

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

What is claimed is:

Claim 1 (withdrawn): A compound to selectively kill a target cell in a patient with reduced systemic toxicity, which comprises a compound of the formula: W-Z-X wherein, X is a therapeutical agent selected from the group consisting of chemotherapeutic agent, antiviral agent, antibacterial agent, antifungal agent and enzyme inhibitor agent; W is a molecule which is adapted to selectively bind said target cell directly or indirectly; and Z is a breakable linker which covalently links W and X together, wherein said linked W remains available for binding to said target cell, whereby said breakable linker releases said therapeutical agent into said target cell.

Claim 2 (withdrawn): The compound of claim 1, wherein said compound when bound to said target cell is internalized into said target cell.

Claim 3 (withdrawn): The compound of any one of claims 1 and 2, wherein said linker is breakable by pH modification, reduction or enzymatic hydrolysis.

Claim 4 (withdrawn): The compound of any one of claims 1 to 3, wherein said chemotherapeutic agent is selected from the group of taxanes, taxanes derivatives, anthracyclines, anthracyclines derivatives, doxorubicin, daunomycin, daunorubicin, adriamycin, methotrexate, mitomycin, epirubicin, nucleoside analogs, DNA damaging agents and tyrphostins.

Claim 5 (withdrawn): The compound of any one of claims 1 to 4, wherein said therapeutical agent is selected from the group of antisense oligonucleotide and cDNA for a gene.

Claim 6 (withdrawn): The compound of claim 4 wherein said taxane is paclitaxel.

Claim 7 (withdrawn): The compound of any one of claims 1 to 3, wherein said chemotherapeutic agent is doxorubicin.

Claim 8 (withdrawn): The compound of claim 1 wherein said molecule is selected from the group of antibody and mimicking molecules thereof, peptides, peptidomimetics, growth factors, hormones, adhesion molecules, viral proteins and functional fragments thereof.

Claim 9 (withdrawn): The compound of claim 8 wherein said antibody is a monoclonal antibody.

Claim 10 (withdrawn): The compound of claim 8, wherein said antibody binds to a specific receptor on said target cell.

Claim 11 (withdrawn): The compound of claim 9 wherein said monoclonal antibody is selected from the group of MC192, 5C3 and a-IR3.

Claim 12 (withdrawn): The compound of claim 1, wherein said compound further comprises a spacer between W and Z and/or between Z and X.

Claim 13 (withdrawn): The compound of claim 12, wherein when W is a primary biologically active molecule indirectly binding to said target cell, said compound further comprises W' which is a secondary biologically active molecule selectively bound to W and adapted to selectively bind said target cell.

Claim 14 (withdrawn): The compound of claim 13 wherein said primary and/or said secondary biologically active molecules is an antibody.

Claim 15 (withdrawn): The compound of claim 14 wherein a primary antibody is of a species and a secondary antibody is of a different species.

Claim 16 (withdrawn): The compound of any one of claims 14 or 15, wherein said antibody is a monoclonal antibody.

Claim 17 (withdrawn): The compound of claim 13 wherein said secondary biologically active molecule is a rabbit-antimouse antibody.

Claim 18 (withdrawn): The compound of claim 1, wherein said compound is of the formula:
6 wherein Y is a spacer selected from the group of alkene, alkyl, methyl, ethyl ester, ethyl glycol and $\text{H}(\text{CH}_2\text{CH}_2\text{O})_n\text{OH}$, n being between 1 and 90.

Claim 19 (withdrawn): The compound of claim 18, wherein said spacer is $(\text{CH}_2)_3$.

Claim 20 (withdrawn): The compound of claim 1, wherein said compound is of the formula I, 7

Claim 21 (withdrawn): The compound of claim 1, wherein Z is 8

Claim 22 (withdrawn): The compound of claim 1, wherein said compound is of the formula II, 9

Claim 23 (withdrawn): The compound of claim 1, wherein said compound is of the formula III, 10

Claim 24 (withdrawn): A therapeutical composition, which comprises a therapeutically effective amount of a compound of any of claims 1 to 23 in association with a pharmaceutically acceptable carrier.

Claim 25 (withdrawn): An anti-cancer composition, which comprises a therapeutically effective amount of a compound of any of claims 1 to 23 in association with a pharmaceutically acceptable carrier, wherein said therapeutical agent is a chemotherapeutic agent.

Claim 26 (withdrawn): A method for treating cancer with reduced effects in a patient, said method consisting in administering a therapeutically effective amount of a compound of any of claims 1 to 23 to a patient, wherein said therapeutical agent is a chemotherapeutic agent.

Claim 27 (withdrawn): Use of the compound of any one of claims 1 to 23 for the manufacture of a medicament for the treatment of cancer with reduced effects in a patient, wherein said therapeutical agent is a chemotherapeutic agent.

Claim 28 (withdrawn): A method for decreasing toxic side effects and increasing selectivity of a chemotherapeutic agent for tumor cells, said method comprising the step of administering to a patient a conjugate comprising a chemotherapeutic agent conjugated to a molecule which is adapted to selectively bind said target cell directly or indirectly, wherein said compound when bound to said target cell is internalized into said cell and to a breakable linker which covalently links said molecule and said chemotherapeutic agent together, wherein said linked molecule remains available for binding said target cell, whereby said breakable linker releases said chemotherapeutic agent into said target cell.

Claim 29 (withdrawn): Use of a chemotherapeutic agent conjugated to a molecule for decreasing toxic side effects and increasing selectivity of a chemotherapeutic agent for tumor cells, said molecule being adapted to selectively bind said target cell directly or indirectly, wherein said compound when bound to said target cell is internalized into said cell and to a breakable linker which covalently links said molecule and said chemotherapeutic agent together, wherein said linked molecule remains available for binding said target cell, whereby said breakable linker releases said chemotherapeutic agent into said target cell.

Claim 30 (cancelled).

Claim 31 (withdrawn): A compound to selectively protect a target cell which comprises a compound of the formula: W-Z-X wherein, X is a protective agent to cells selected from the group consisting of: enzyme inhibitors, ligands of nuclear receptors, vitamin D, vitamin E and analogs thereof, estrogen and analogs thereof and inhibitors of the apoptotic cascade; W is a biologically active molecule which is adapted to selectively bind said target cell directly or indirectly; and Z is a linker which covalently links W and X together, wherein said linked W remains available for binding said target cell, whereby said linker releases said therapeutic agent into said cell and whereby said compound is providing a patient with a reduced systemic toxicity.

Claim 32 (withdrawn): The compound of claim 31, wherein said protective agent is an enzyme inhibitor agent.

Claim 33 (withdrawn): The compound of claim 32, wherein said enzyme inhibitor agent is a caspase inhibitor agent.

Claim 34 (withdrawn): A method for decreasing toxic side effects to non-tumor cells, said method comprising the step of administering to a patient a conjugate comprising a protective agent conjugated to a molecule which is adapted to selectively bind said non-tumor target cell directly or indirectly, wherein said compound when bound to said non-tumor target cell and to a breakable linker which covalently links said molecule and said protective agent together, wherein said linked molecule remains available for binding said target cell, whereby said breakable linker releases said protective agent into said cell and whereby said protective agent internalized in said cell is protecting said cell from subsequent toxicity by a chemotherapeutic agent which is therefore decreasing toxic side effects.

Claim 35 (currently amended). A method of treating a patient with a tumor comprising ~~for by-passing tumor cell drug resistance mediated by p-glycoprotein pump (PGP) thus for treatment of drug-resistant tumor cells, including drug-resistant tumor cells mediated by p-glycoprotein pump,~~ said method comprising the step of administering a compound to selectively kill ~~[[a]]~~ said tumor cells in ~~[[a]]~~ said patient, said compound ~~having reduced systemic toxicity and having the~~ formula:

W-Z-X

wherein,

X is a chemotherapeutic agent selected from the group consisting of: doxorubicin; and paclitaxel;

W is ~~a targeting agent selected from the group consisting of a monoclonal antibody and a ligand adapted to~~ monoclonal antibody which selectively binds to a polypeptide expressed on the surface of said tumor cells; and

Z is a breakable linker which covalently links W and X together, wherein said W, when linked to Z, remains available for binding to said tumor cells, said breakable linker being cleavable in the cells for releasing X into said tumor cells, whereby the release of X into said tumor cells is cytotoxic and selectively kills said tumor cells, including drug-resistant tumor cells mediated by p-glycoprotein pump, thereby treating said patient ~~said compound is avoiding membrane diffusion and/or permeability route and thus bypassing resistance of tumor cells by the PGP to enter into said cells.~~

Claim 36-37 (canceled).

Claim 38 (new): A method according to claim 35, wherein said polypeptide expressed on the surface of said tumor cells is selected from the group consisting of: p75 neurotrophin receptor (p75), neurotrophic receptor tyrosine kinase (TrKA) or insulin-like growth factor receptor, type 1 (IGF-1R).

Claim 39 (new): A method according to claim 35, wherein said monoclonal antibody is a monoclonal antibody selected from the group consisting of: α -IR3; 5C3; and MC192.